

Combinatorial compound library

- 15,000 compounds screened; collection growing
- Novel “drug like” molecules by Lipinski’s “rule of 5”
- Based on 125 templates, 200 congeners each

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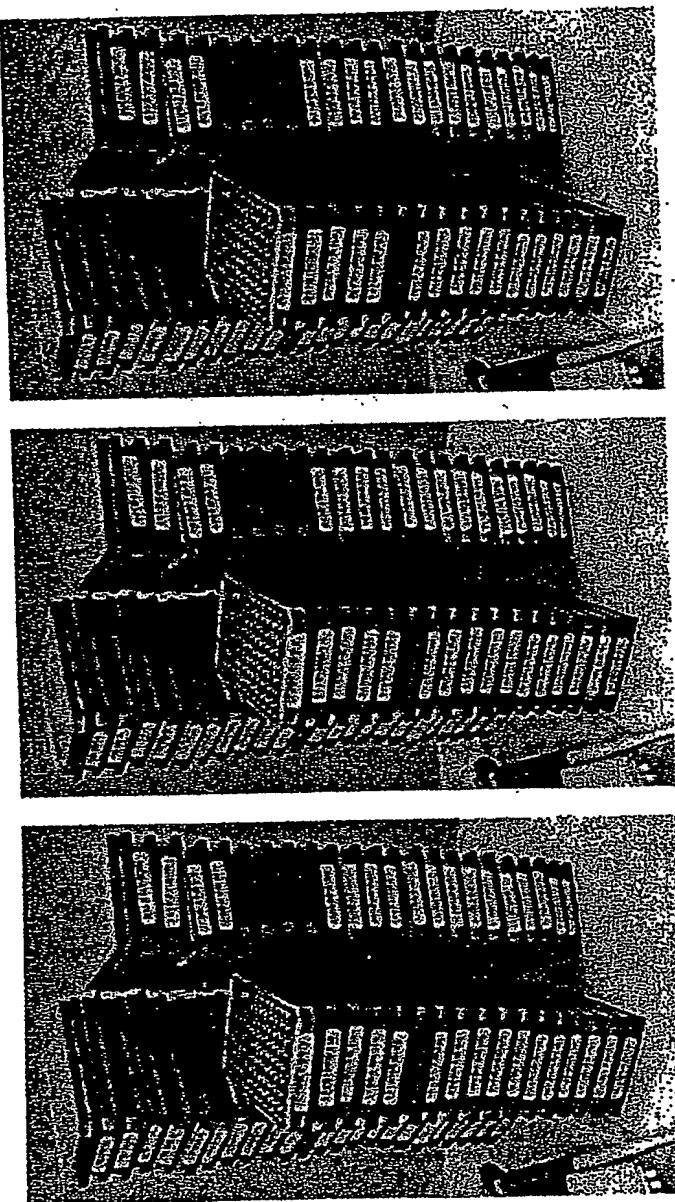
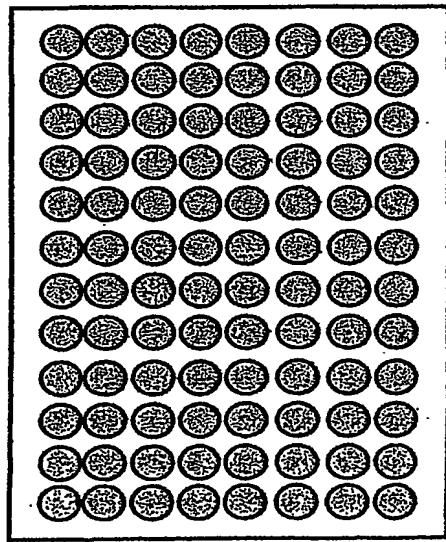


Figure 1

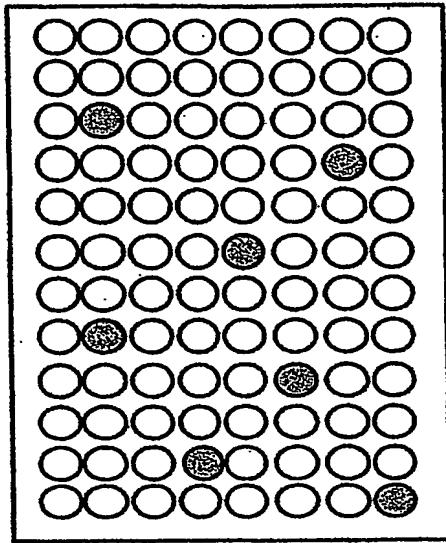
Screening scheme

assay mix/compound/mix

(T90)



90 min at 37°C



1.5×10^4 neutrophils/well
incubate with test agents
37C for 30 min; add TNF

Inhibitors of TNF specific
signaling molecules

Toxicity to neutrophils[]

Inhibitors of the assay itself (HRP)
Intrinsic fluorescence

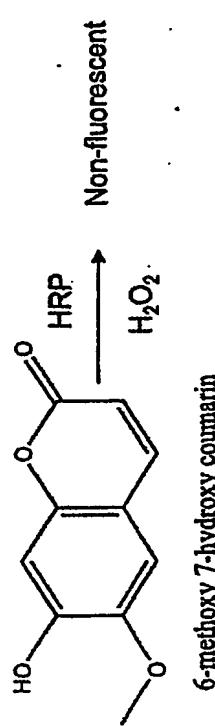


Figure 2

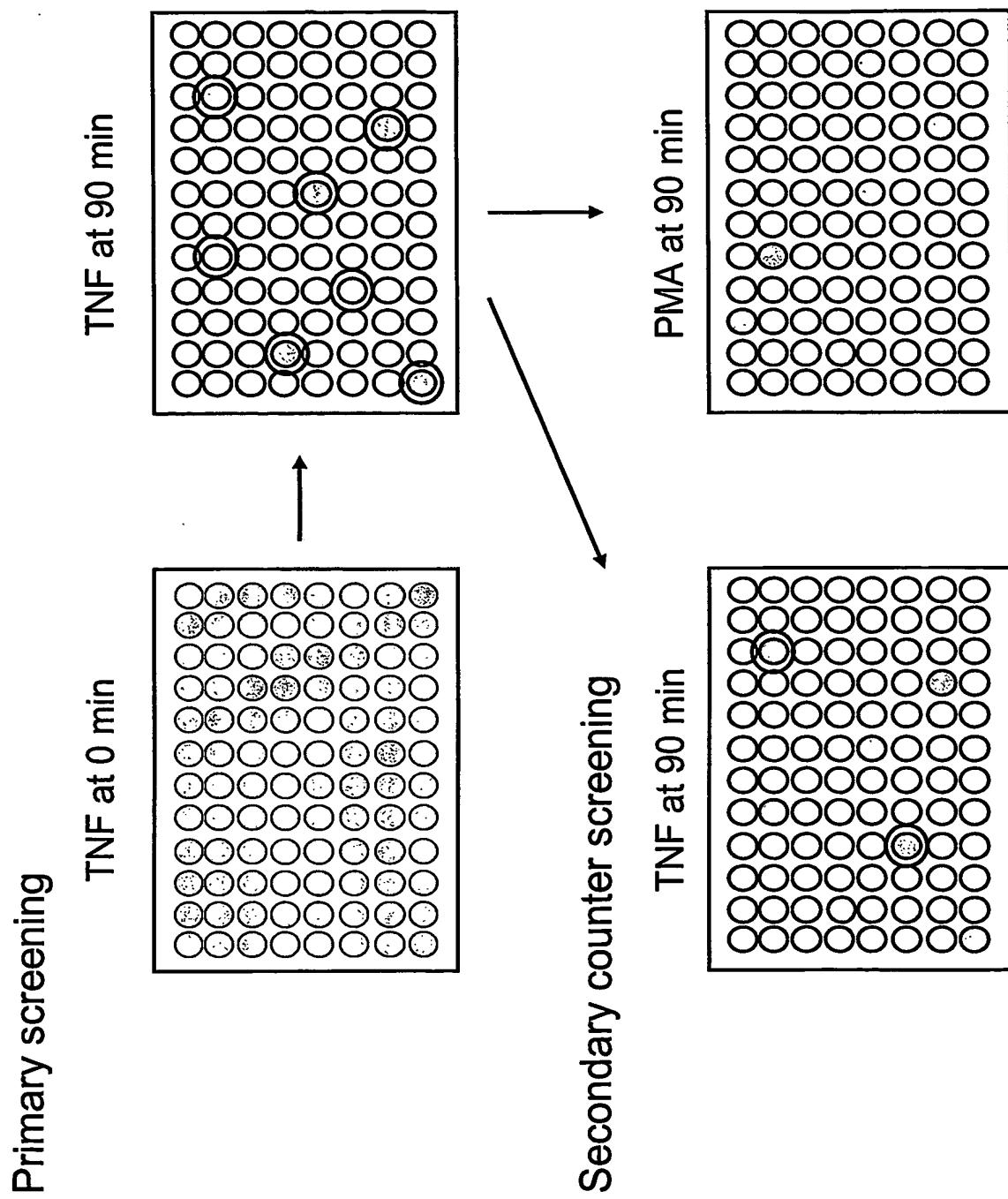
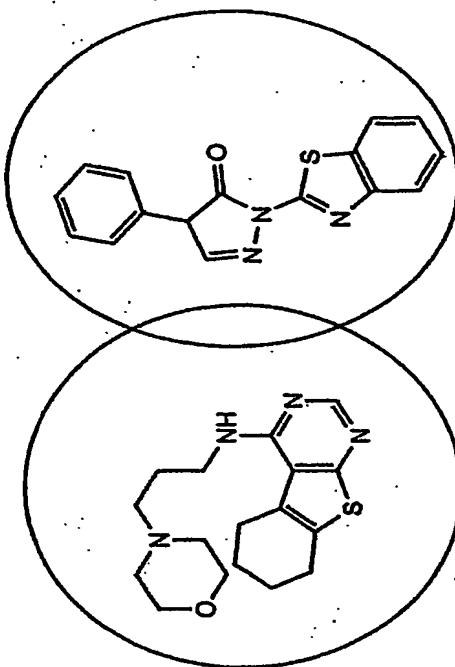
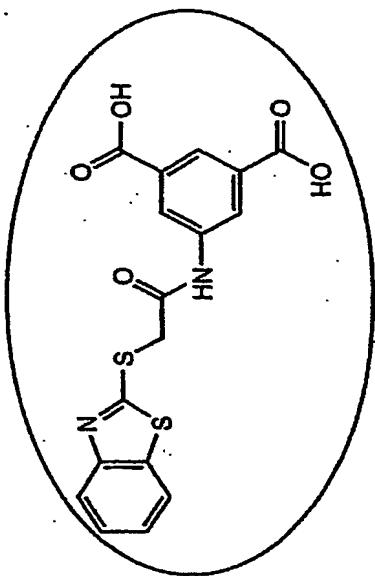


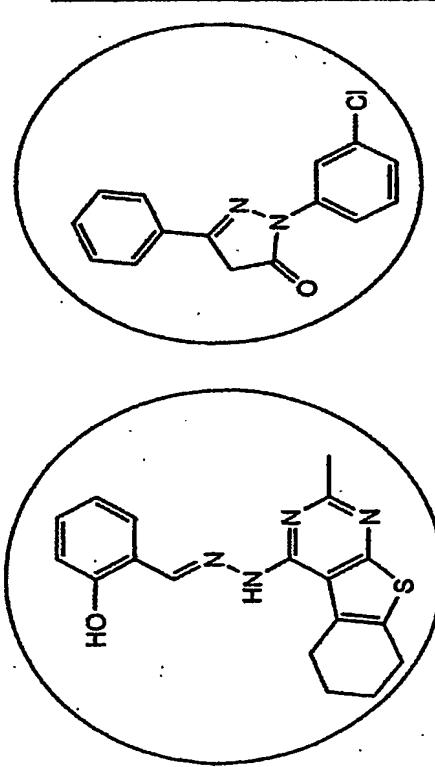
Figure 3

Inactive controls

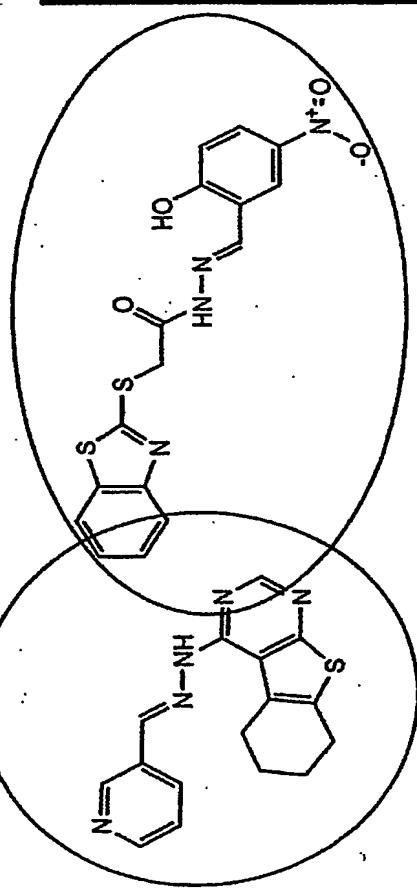
49G04 (CL0651) 37A03(CL0326)



120A07 (CL0338)

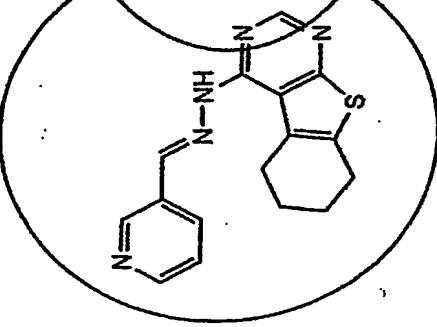
Active inhibitors

53F03 (CL0326)



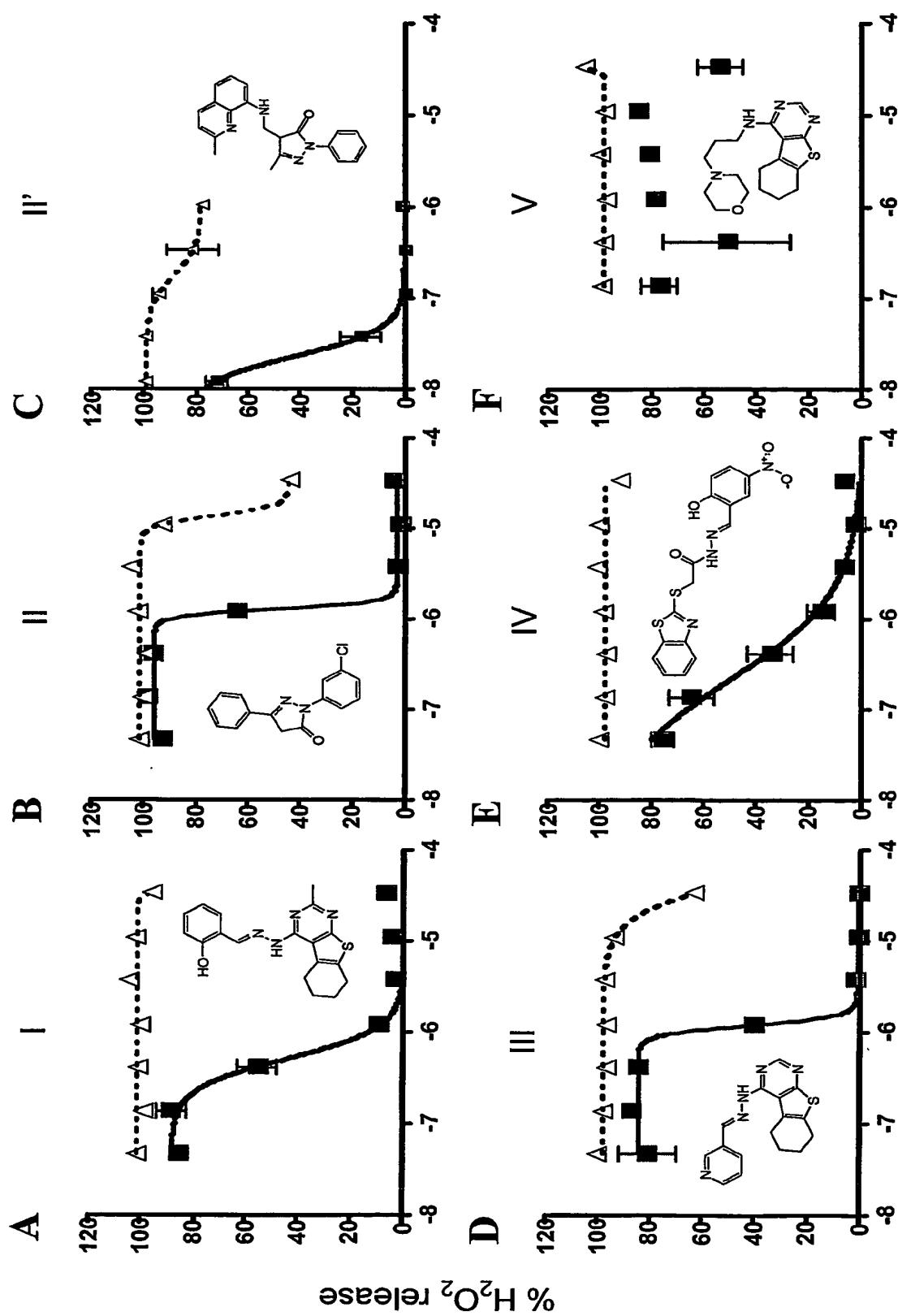
109G01(CL0338)

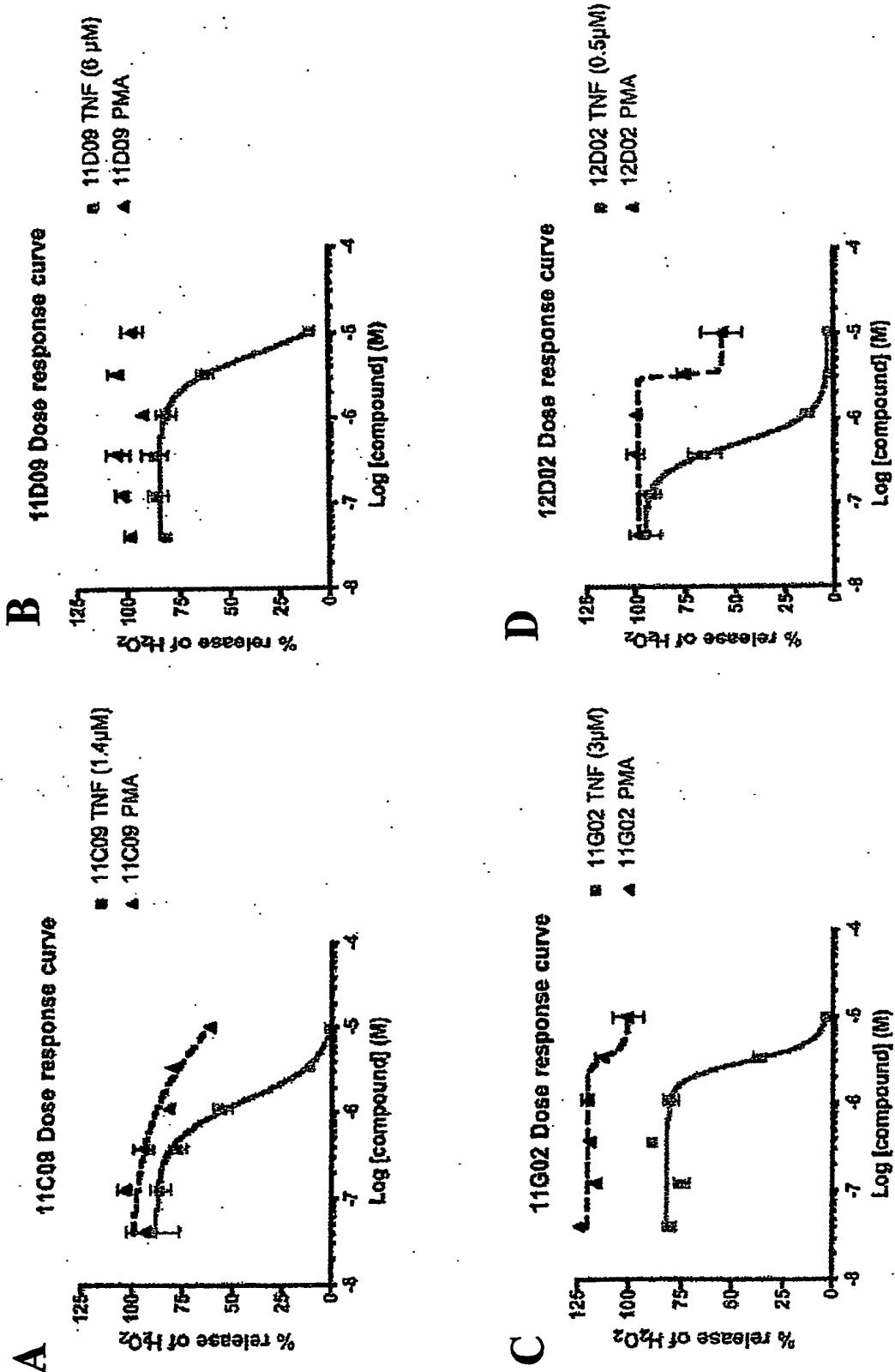
23G01(CL0651)



55D01(CL0651)

Figure 4

**Figure 5**Log₁₀ [compound] M

**Figure 6**

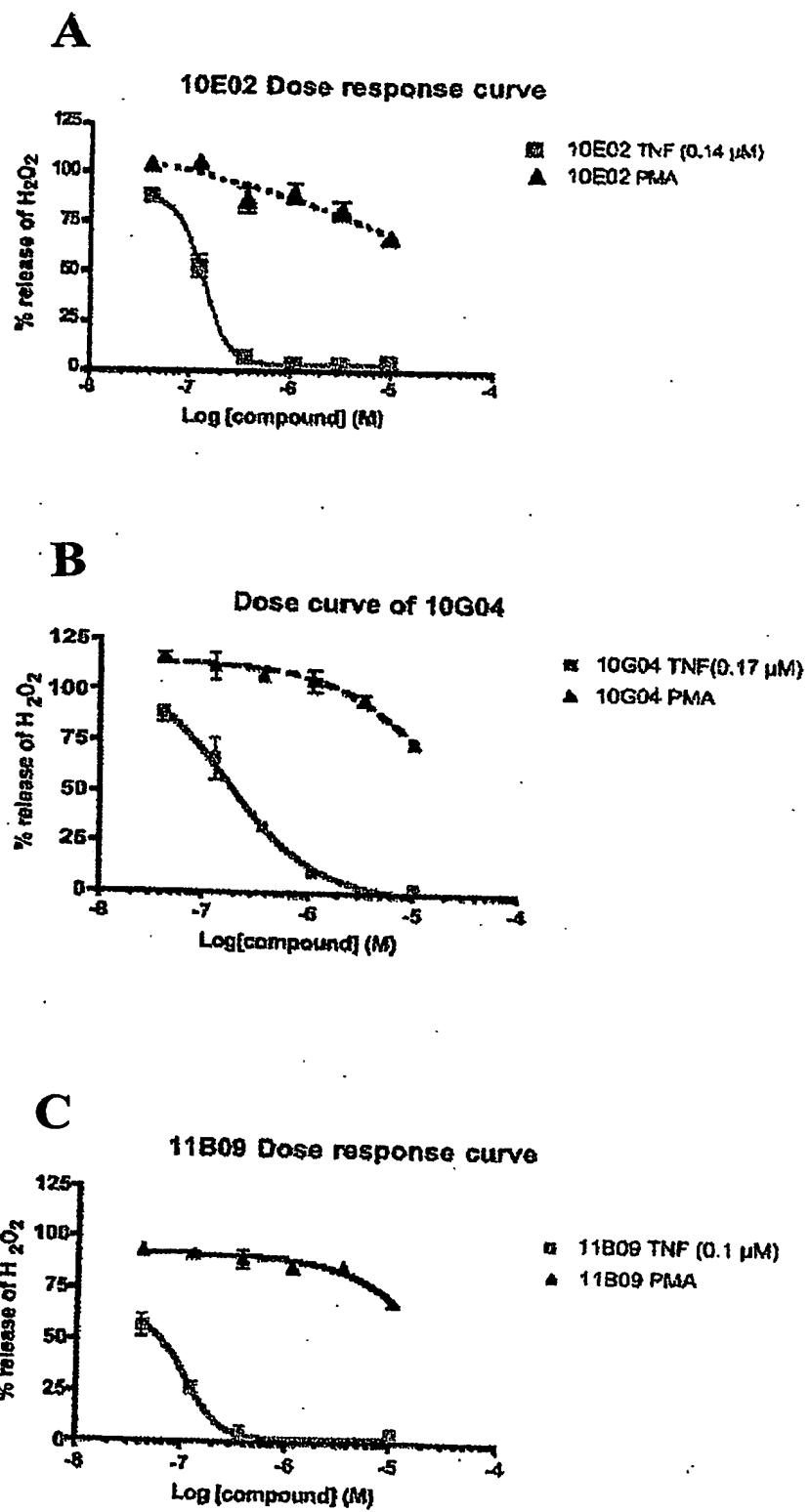


Figure 7

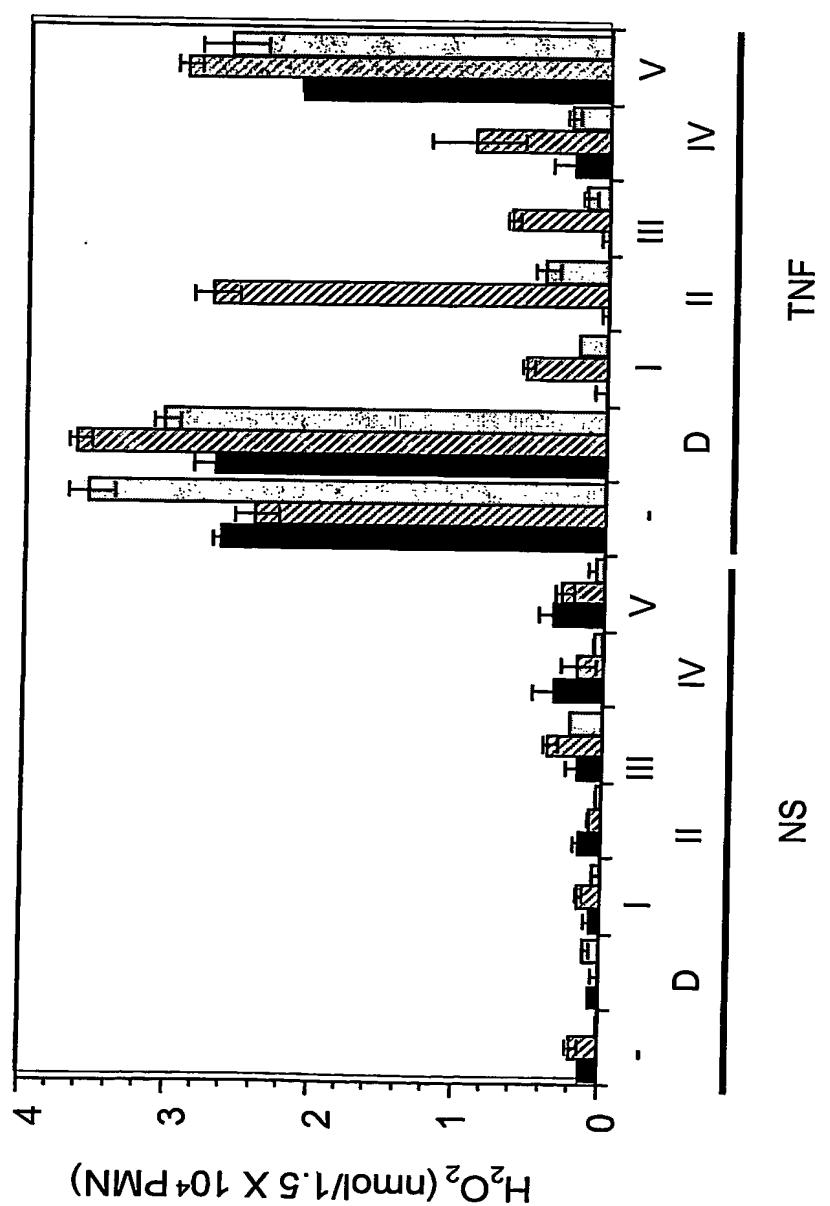


Figure 8

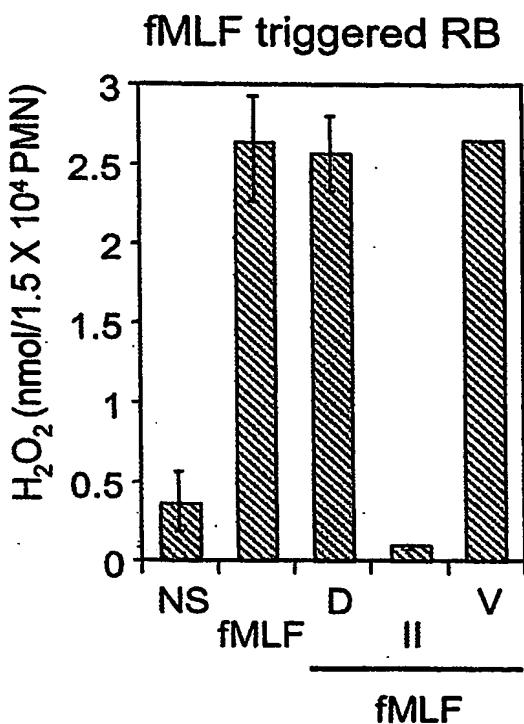


Figure 9A

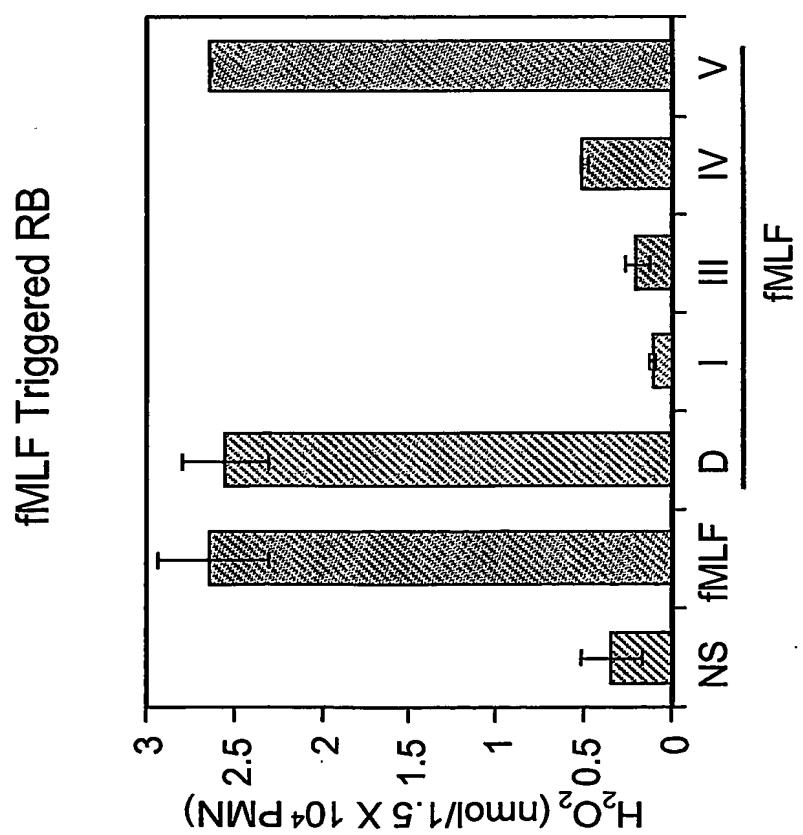


Figure 9 B

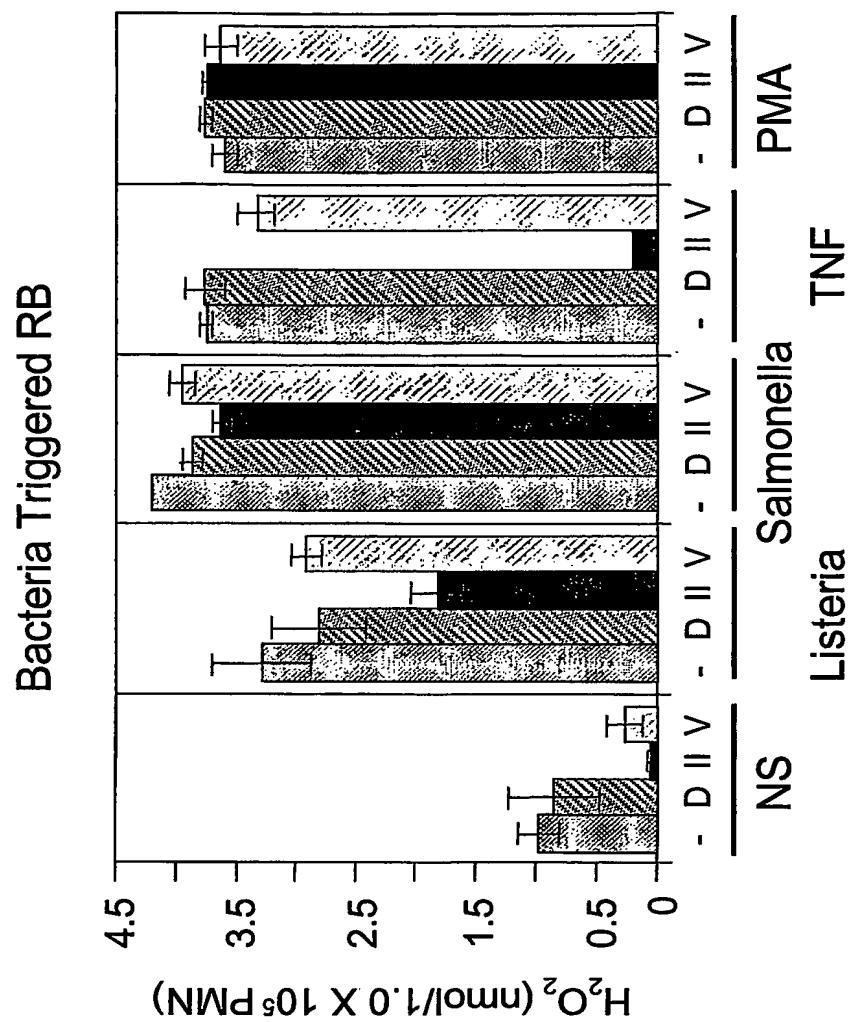


Figure 10A

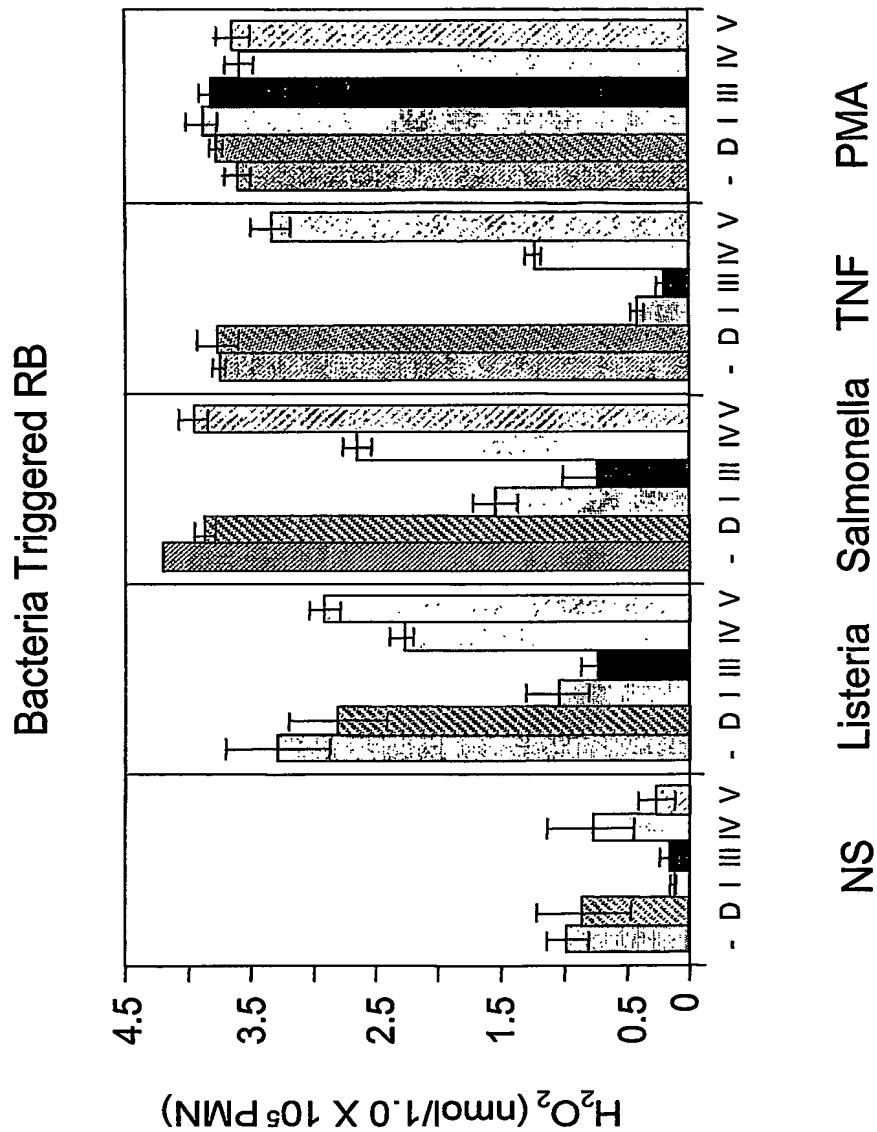


Figure 10B

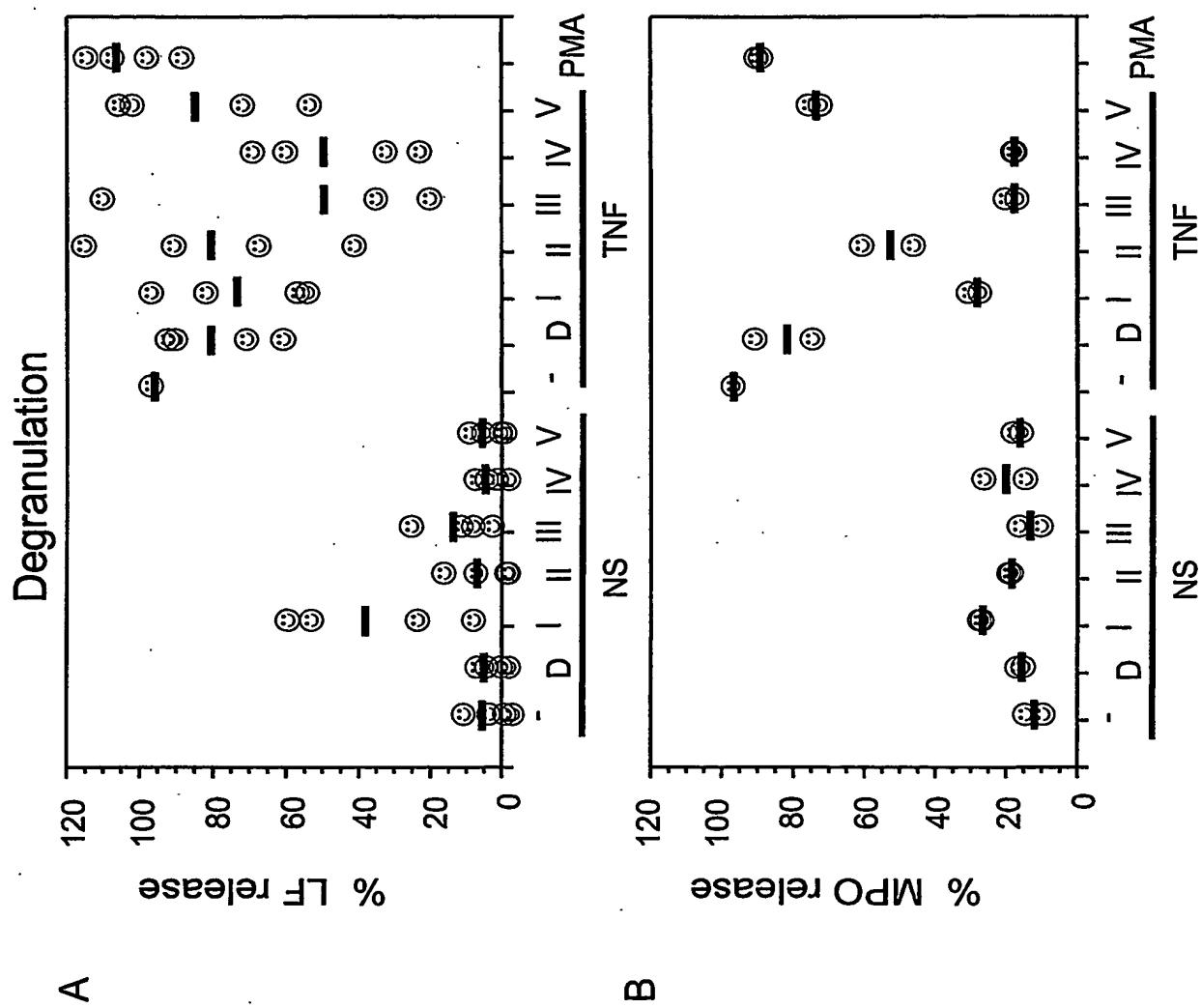


Figure 11

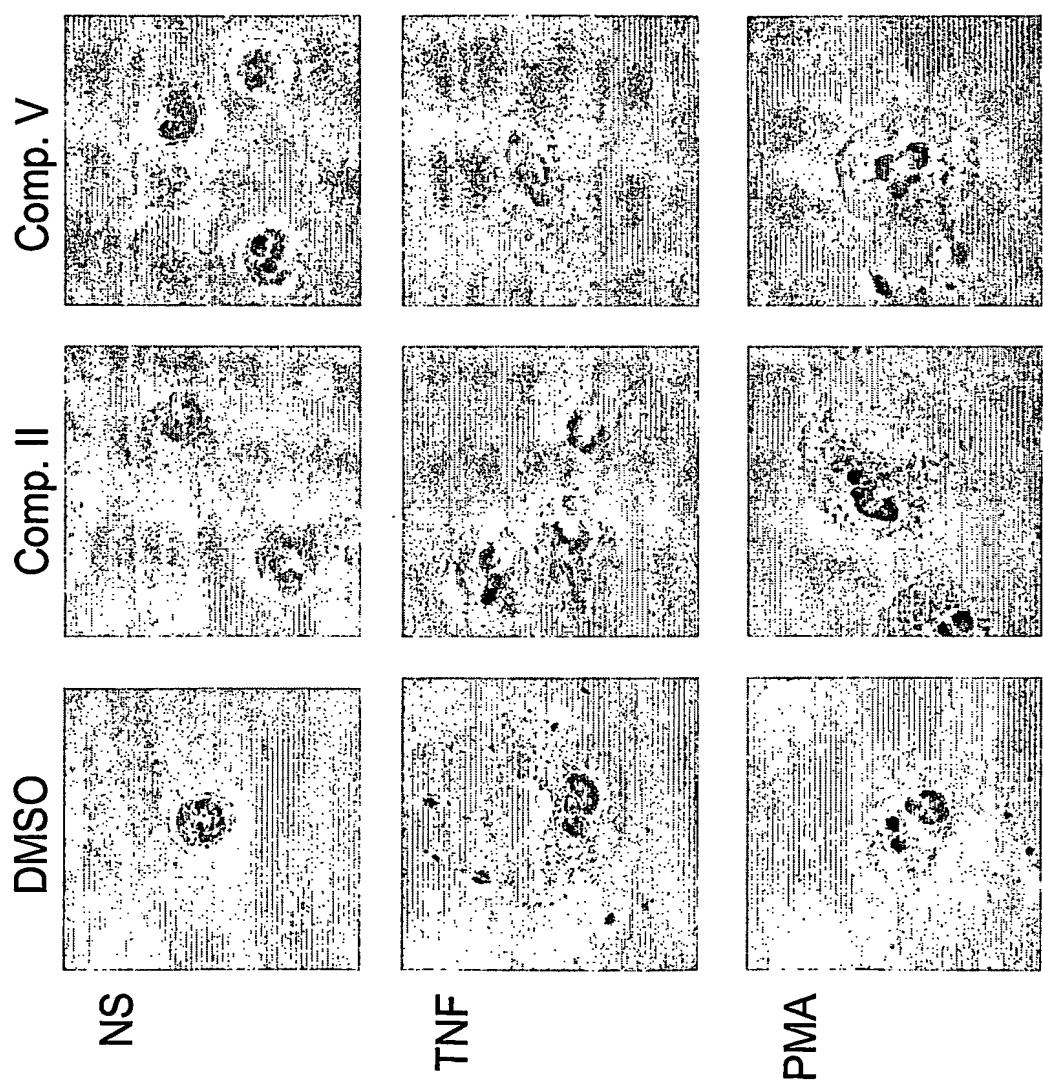


Figure 12A

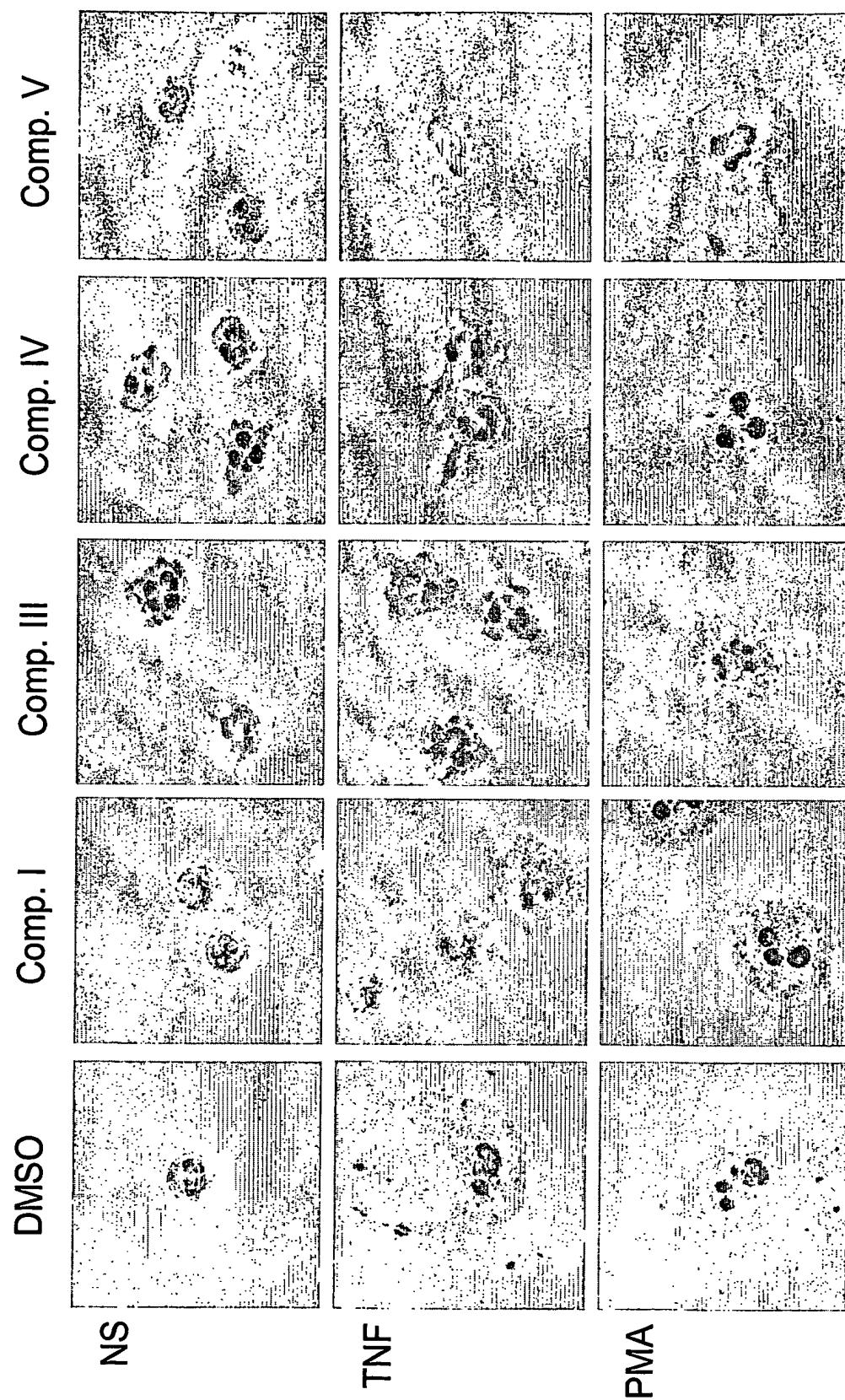
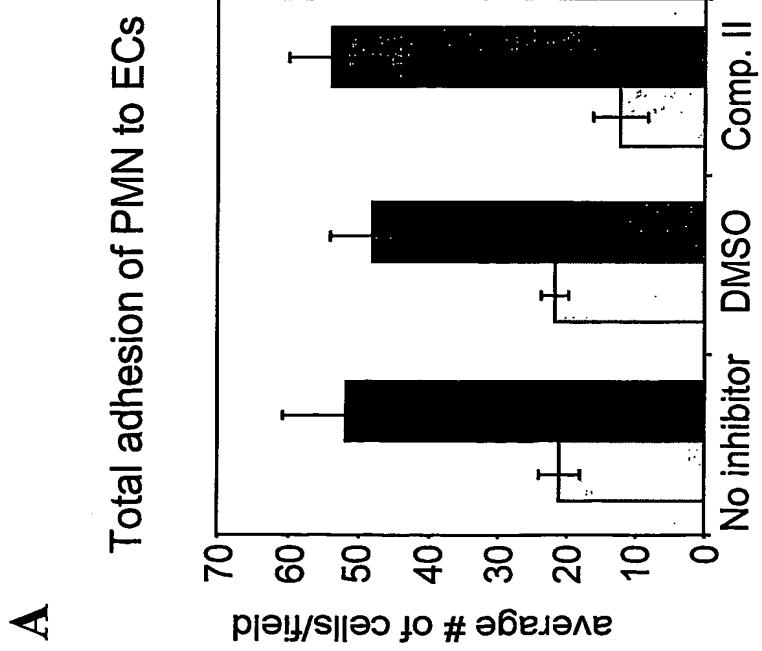


Figure 12B



B

TEM of PMN through ECs

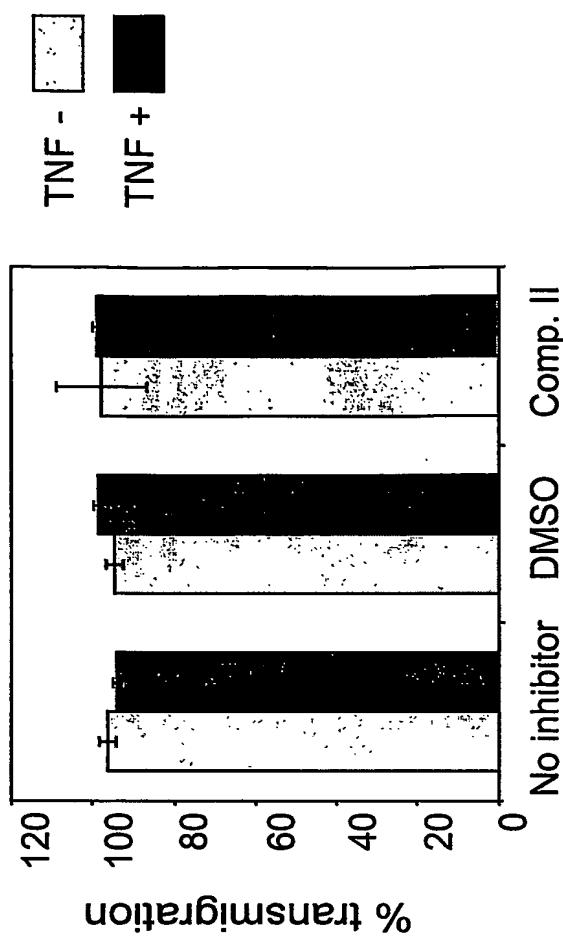
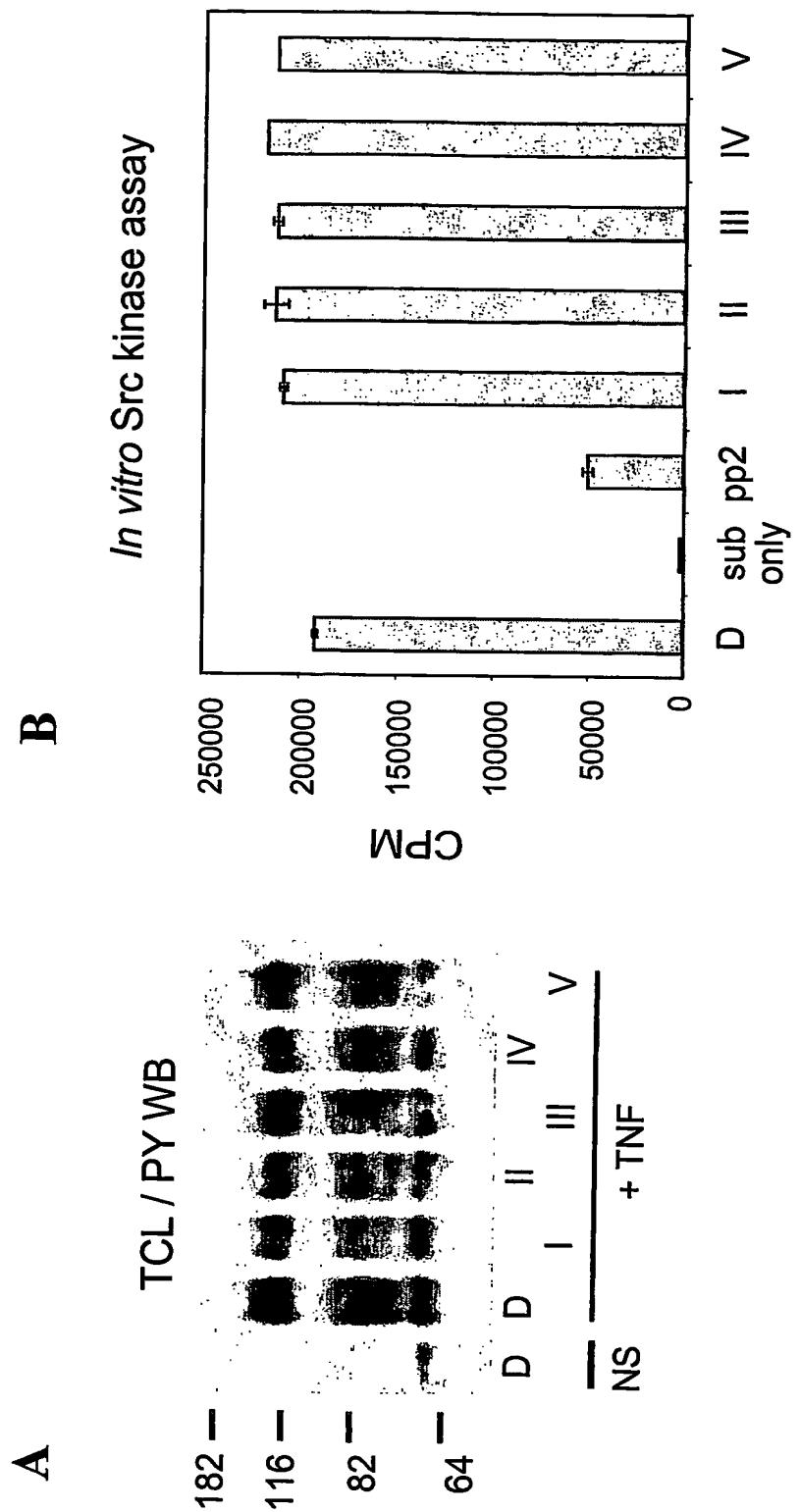


Figure 13

**Figure 14A-B**

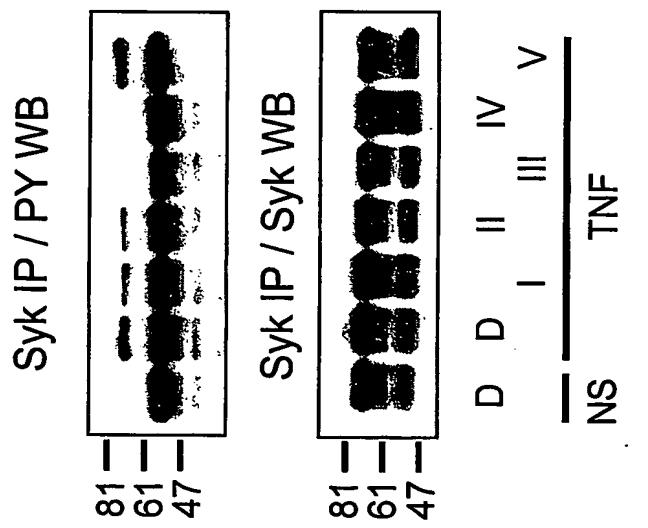
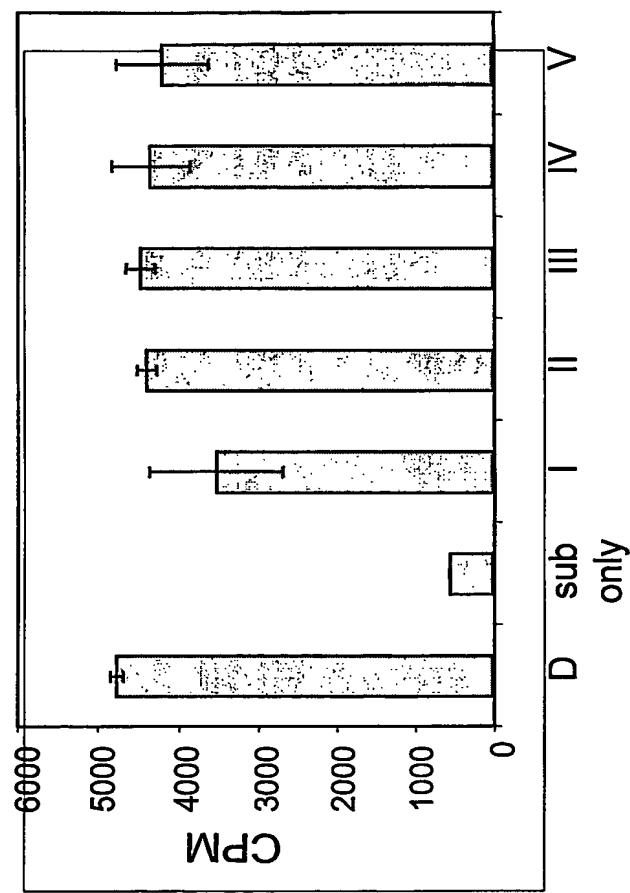


Figure 14C

In vitro Syk Kinase Assay**Figure 14D**

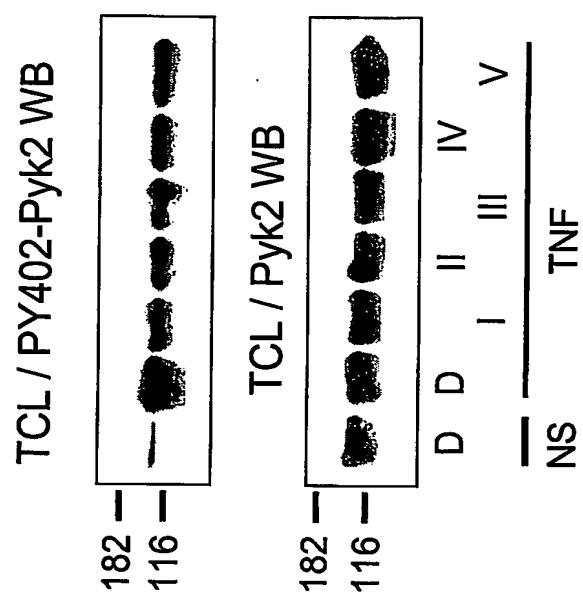


Figure 15

Phagocyte oxidase (phox) (NADPH oxidase)

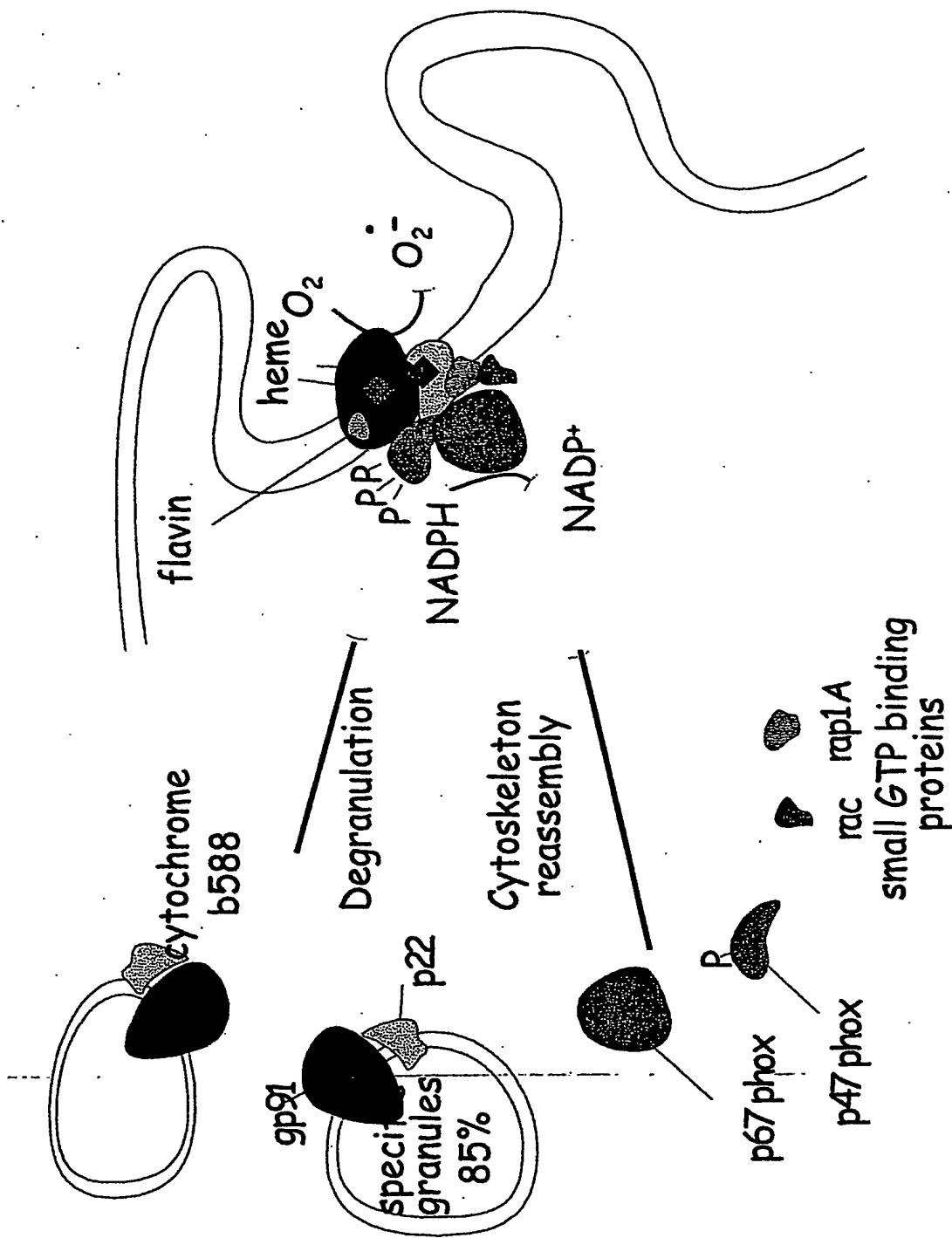


Figure 16

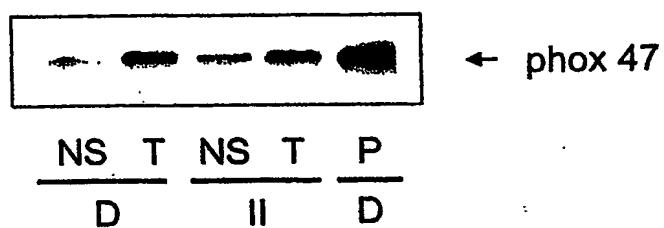


Figure 17

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